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Access routes and reported decision criteria for lumbar epidural drug injections: a systematic literature review

Andreisek, Gustav ; Jenni, Maja ; Klingler, Dominic ; Wertli, Maria ; Elliott, Marina ; Ulbrich, Erika J
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Abstract: **PURPOSE:** To review lumbar epidural drug injection routes in relation to current practice and the reported criteria used for selecting a given approach. **MATERIAL AND METHODS:** This was a HIPPA-compliant study. Employing a systematic search strategy, the MEDLINE and EMBASE databank as well as the Cochrane Library were searched for studies on epidural drug injections. The following data were noted: access route, level of injection, use of image guidance, and types and doses of injected drugs. Justifications for the use of a particular route were also noted. Data were presented using descriptive statistics. **RESULTS:** A total of 1,211 scientific studies were identified, of which 91 were finally included (7.5 %). The interlaminar access route was used in 44 of 91 studies (48.4 %), the transforaminal in 37 of 91 studies (40.7 %), and the caudal pathway in 26 of 91 studies (28.6 %). The caudal pathway was favored in the older studies whereas the transforaminal route was favored in recent studies. Decision criteria related to correct needle placement, concentration of injected drug at lesion site, technical complexity, costs, and potential complications. Injection was usually performed on the level of the lesion using local anesthetics (71 of 91 studies, 78.0 %), steroids (all studies) and image guidance (71 of 91 studies, 78 %). **CONCLUSIONS:** The most commonly used access routes for epidural drug injection are the interlaminar and transforaminal pathways at the level of the pathology. Transforaminal routes are being performed with increasing frequency in recent years.

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Conclusions The most commonly used access routes for epidural drug injection are the interlaminar and transforaminal pathways at the level of the pathology. Transforaminal routes are being performed with increasing frequency in recent years.

On behalf of the Lumbar Spinal Stenosis Outcome Study (LSOS) Working Group Zurich.

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Keywords Lumbar spine · Stenosis · Epidural · Intervention · Injection

Introduction

The epidural injection of drugs via different routes is one of the most commonly performed procedures in the treatment of chronic low back pain and has shown a steady increase over the past decades. In the Medicare population, the number of lumbar epidural injections quadrupled within 7 years (1994–2001) [1]. Epidural injections are used to treat lumbosacral radicular pain, but also in patients with lumbar spinal stenosis and other degenerative changes. Local anesthetics and steroids, or steroids alone are commonly used substances. Local

anesthetics are believed to impede the nociceptor transmission and interrupt the pain spasm-cycle whereas steroids are thought to reduce inflammation by inhibiting either synthesis or release of pro-inflammatory mediators [2].

The discussion is still ongoing as to whether epidural injections are effective. Nine systematic reviews have evaluated the benefits and adverse effects of epidural injections. Most of the reviews conclude that epidural injections relieve pain for days or even weeks, whereas long-term pain relief is rarely achieved [3]. As a result, most current guidelines do not recommend epidural injections. However, there are also several ongoing, unpublished trials that might reveal positive long-term effects of epidural injections [3, 4].

Uncertainty also prevails regarding the most appropriate route of access to the lumbar epidural space. The three possible routes are the interlaminar, the transforaminal, and the caudal pathways [5]. Currently, there is no consensus in the literature on which access route should be used. Therefore, this paper aimed to review the current practice for epidural injections as well as the reported decision criteria used for choosing a particular access route into the epidural space.

Materials and methods

This is a structured literature review study compliant with the current Declaration of Helsinki and Health Insurance Portability and Accountability Act (HIPAA). No ethical review board approval was necessary according to local laws and institutional regulations. There was no funding of this study.

Literature search

As a preliminary step, a literature search for all relevant publications about epidural drug injection in patients with low back pain was performed between November 2011 and March 2012, by a professional librarian (initials blinded for the review process, 20 years' experience in literature search with long experience utilizing MEDLINE, EMBASE, and the Cochrane Library). The search attempted to identify all systematic reviews, and experimental and observational studies published in English or German. The librarian developed the search strategy. The focus was on epidural injections of steroids and local anesthetics via interlaminar, transforaminal, or caudal access routes. The search strategy for Medline is shown in Table 1.

Selection criteria

Following the literature search, results from all three databases were combined and duplicate publications were removed. All randomized and observational studies reporting on the site of injection in patients with lower back pain were included, but studies with fewer than ten patients were rejected.

Table 1 Example for the literature search in Medline (Ovid) using a systematic and standardized search strategy that was developed by a professional librarian. Please note that abbreviations are not self-explanatory. These are commands used for searches in Medline or other databases

Terms	Result
1 Low back pain/	11,565
2 (("low back" or discogenic or ((spinal or lumbar) adj3 radicular)) adj3 pain).ti,ab.	14,526
3 (herniation or radiculitis).ti,ab.	10,977
4 Intervertebral displacement/	14,528
5 Disc adj3 (hernia* or prolapse* or slip*).ti,ab.	5,465
6 Radiculopathy/	3,039
7 (lumbal adj3 spinal adj3 stenosis).ti,ab.	5
8 (lumbosacral adj3 radiculopathy).to,ab.	191
9 Or/3-8	24,782
10 Pain.mp. or Pain/	400,577
11 9 and 10	7,073
12 1 or 2 or 11	23,326
13 Injections, epidural/	1,853
14 Anesthesia, epidural/	10,684
15 (local* or lumb* or epidural*) adj3 inject*).ti,ab.	10,774
16 ((lumb* or epidural*) adj3 (inject* or anesthetic*)).ti,ab.	3,114
17 Or/13-16	21,969
18 12 and 17	802
19 Limit 18 to "all child (0 to 18 years)"	55
20 Limit 18 to case reports	155
21 18 not (19 or 20)	597
22 Limit 21 to (English or French or German)	575

Data extraction

Year of publication, number of included patients, age and age range of the patients, main patient inclusion criteria, and primary outcome parameters, were extracted by two authors (initials blinded for review process, 1 and 25 years' experience in epidemiological studies, respectively). The access route for drug application, the level of injection for interlaminar and transforaminal route, use of any image guidance or image control during or after the injection (e.g., by fluoroscopy, CT, ultrasound, or others), as well as types and doses of injected drugs, were also extracted. In addition, all included publications were searched in detail for arguments given by the authors for why they selected the given access route for epidural drug application.

Data synthesis and statistical analysis

All data were summarized using spreadsheets (Excel, Microsoft, Seattle, WA, USA), and are presented using descriptive statistics. Access route selection criteria are

described qualitatively. No statistical calculations were performed in this structured literature review study.

Results

Literature

The initial structured literature searches resulted, after de-duplication, in 1,211 papers which referred directly or indirectly to epidural injection. After reading all titles and abstracts, 1,077 of 1,211 publications (88.9 %) were excluded. Full texts from the remaining 134 of 1,211 papers (11.1 %) were ordered. After reading the 134 studies, 91 (7.5 %) fulfilled the inclusion criteria. Of these 91 studies, 59 were randomized controlled trials [6–64] and 32 were observational studies [65–96]. All studies were published between 1971 and 2011, with the majority (60 of 91, 65.9 %) published in the last decade (Fig. 1).

Patient population and inclusion criteria

On average, 85 patients were included per study. The smallest study involved ten patients [75] and the largest study involved 306 [11]. The mean age of the patients over all studies was 50 years. The mean of the youngest study group was 28 years [22] and the mean of the oldest study group was 78 years [69].

Inclusion criteria in these 91 studies were rather homogeneous as the majority of studies (75 of 91, 82.4 %) focused on patients with radicular symptoms. Some studies also included patients with lumbar spinal stenosis, chronic back pain refractory to usual analgesics, or complaints after spinal surgery (24, 30, and seven of 91 studies; 26.4, 33.0, and 7.7 %, respectively).

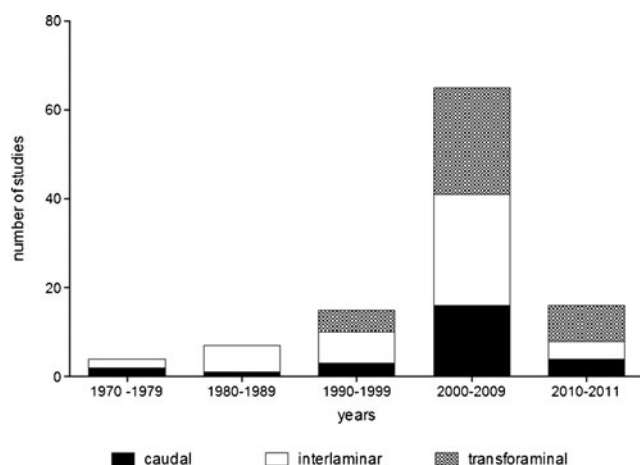


Fig. 1 Bar chart showing the number of publications per decade for each different approach (caudal, interlaminar, and transforaminal injection pathway)

Route of injection

In 44 of 91 studies (48.4 %), drugs were injected via the interlaminar approach (Fig. 2), while 37 (40.7 %) used the transforaminal route (Fig. 3). The caudal approach was chosen in 26 of the 91 (28.6 %) studies (Fig. 4). Two studies applied all three routes to compare the effects [6, 93]. Two other studies compared the effects on the outcome of caudal and transforaminal routes [73, 85], and two studies compared the caudal with the interlaminar approach [42, 50]. A further eight studies compared the transforaminal route to the interlaminar injection site [25, 36, 38, 51, 61, 91, 92, 94].

Level of injection in relation to level of lesion

In 20 of the 44 studies that evaluated the effect of the interlaminar route, the drugs were injected at the level of the lesion. Only three studies performed the injection at a level above (cranial) the level of the lesion [7, 16, 26]. The level of injection in relation to the causal lesion was not declared or remained unclear due to poor description in 21 studies.

In 33 of 37 studies that evaluated the effect of the transforaminal approach, the drugs were injected on the level where the involved nerve left its foramen. In two studies [6, 30], drugs were injected via the preganglionic route, as first described by Lew et al. [97]. One study used a retrodiscal [48] approach, while another used the intradiscal approach [25].

In all 26 studies that investigated the caudal approach, the needle was inserted via the sacrococcygeal ligament through the hiatus sacralis. No technical differences with regard to the site or level of injection were found.

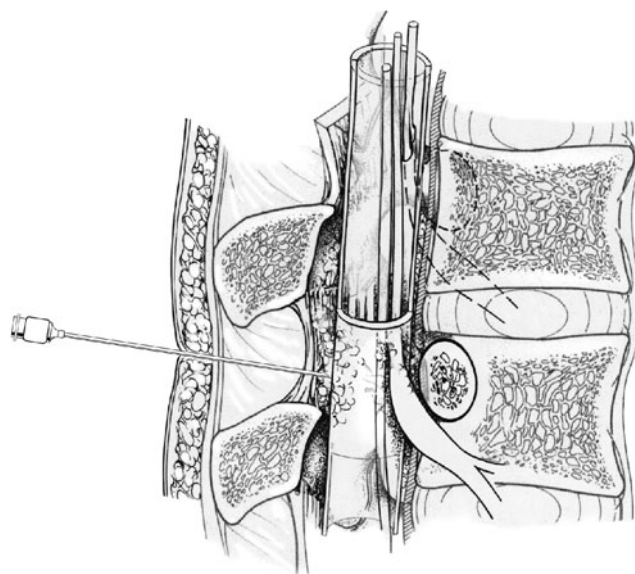


Fig. 2 Anatomic drawing illustrating the access route for interlaminar epidural injections at the lower spine. Sagittal view is provided

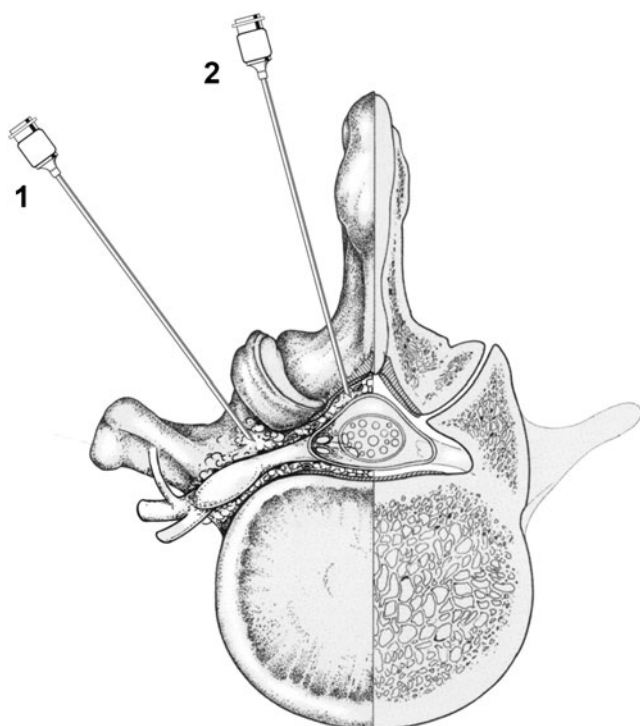


Fig. 3 Anatomic drawing illustrating the access routes for transforaminal epidural injections (1) and interlaminar epidural injections (2) at the lower spine. Transaxial view is provided

Types and doses of injected drugs

Steroids were injected into the epidural space in all studies. Methylprednisolone was the most frequently applied steroid (43 of 91 studies, 47.3 %), followed by triamcinolone (29 of 91 studies, 31.9 %). The dosages ranged from 40–120 mg for methylprednisolone, and 10–80 mg for triamcinolone, per injection. Other steroid preparations included betamethasone (14 of 91 studies, 15.4 %), dexamethasone (four of 91 studies, 4.4 %) and cortivazol (two of 91 studies, 2.2 %).

Local anesthetics were used in 70 of 91 studies (76.9 %). The most often used substances were bupivacaine (31 of 91 studies, 34.1 %) and lidocaine (29 of 91 studies, 31.9 %). Three studies (3.3 %) used non-steroidal analgesics or opioids [7, 55, 86] and two (2.2 %) used an oxygen-ozone gas mixture [11, 25].

Injection under imaging control

In three of 44 studies (6.8 %) using the interlaminar pathway, injections were performed under CT-guidance (Fig. 5) and in 17 of 44 studies (38.6 %) under fluoroscopic control. The remaining 24 studies did not use image guidance. All 37 transforaminal injections were performed under image control, four of them CT-guided (Fig. 6) and 33 of them under fluoroscopic control (10.8 and 89.2 %). For the caudal

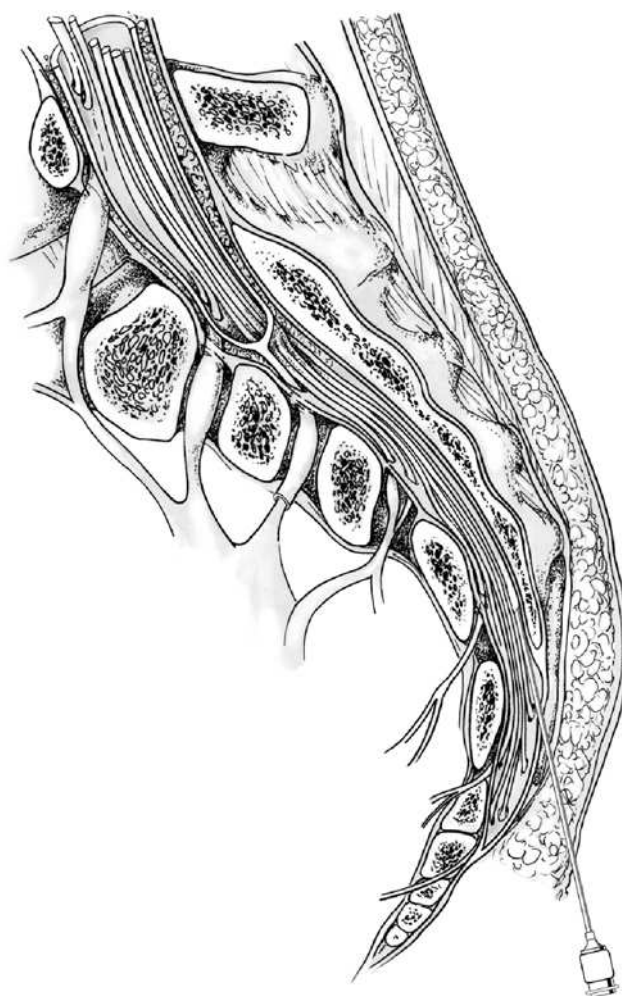


Fig. 4 Anatomic drawing illustrating the access route for caudal epidural injections at the lower spine. Sagittal view is provided

approach, fluoroscopic guidance was used in 13 of 26 studies (50 %), ultrasound control in two of 26 studies (7.7 %), and no imaging control was used in the remaining 11 of 26 studies (42.3 %).



Fig. 5 A 51-year-old male patient with chronic low back pain. Interlaminar access route. Transaxial CT image (slice thickness 3 mm) at the level L4/5 shows needle placement and iodinated contrast within the epidural space. Contrast was injected to proof correct position of needle tip prior to injection of local anesthetics and steroids



Fig. 6 A 78-year-old female patient with chronic low back pain. Transforaminal access route. Transaxial CT image (slice thickness 3 mm) at the level L4/5 shows iodinated contrast along the left L4 nerve root. Contrast was injected to proof correct position of needle tip prior to injection of local anesthetics and steroids

Primary outcome measures

Changes in pain scores, mainly by VAS (visual analog scale), were measured in 77 of 91 studies (84.6 %). Outcome measures were evaluated via the distribution of contrast media in seven studies (7.7 %) [68, 69, 74, 75, 79, 83, 84], and by degree of disability in another 42 studies (46.2 %).

Arguments for selection of injection route

Fifty-four of 91 (59.4 %) studies provided explanations for the choice of injection route. Decision criteria related to the correct needle placement, concentration of injected drug at lesion site, technical complexity of the procedure, costs, and potential complications (Table 2). Detailed analysis of the studies revealed that the caudal approach was the most frequently chosen injection route in older studies whereas the transforaminal route is the most prevalent today (Fig. 1). The remaining 37 studies (40.7 %) provided no justification for the choice of injection route.

Discussion

The discussion is still ongoing as to whether epidural injections are effective or not and if so, for how long. Recently published data on fluoroscopically guided and blind lumbar epidural injections in the management of low back and lower extremity pain have at least shown good evidence for procedures performed under image guidance [98, 99]. However, to the best of our knowledge, only a few studies have evaluated the different access routes for epidural injections. Benyamin et al. [99] discussed the strengths and limitations of different routes but did not perform a systematic analysis of use frequency or assess the criteria authors used to select a given route [99].

This systematic review found that the interlaminar and the foraminal pathway were used almost equally often, namely in

about three fourth of all studies. Interlaminar epidural injections are considered non-specific since the injectate (usually local anesthetics and/or steroids) is free to extend within the posterior epidural space with possible flow anteriorly, cephalad, and caudad [100]. Epidural ligaments or scar tissue might hamper the injectate's extension, but otherwise it can reach multiple areas and nerve roots. Limitations of this access route include extra-epidural needle placement (rare with fluoroscopically guided procedures), preferential flow of the contrast agent towards a non-desired direction, needle deviation to the non-dependent side, difficulty entering the epidural space, potential risk of dural puncture and very rarely, epidural hematoma or spinal cord injury [99, 101]. Transforaminal epidural injections are usually considered to be specific since the injectate is administered in the area where a specific nerve root is leaving the neuroforamen, the typical site of nerve root compression. Using this access route, selected nerves can be targeted. The most commonly cited theory in favor of the transforaminal access route is to place the anti-inflammatory steroid medication as close as possible to the point of nerve root compression. Limitations of the transforaminal access route include misplacement of the needle, intravascular injection, and, when done without fluoroscopic control, the theoretical risk of injuries to the aorta or ureter [102, 103]. Another theoretical risk includes spinal cord injury including severe complications such as paraplegia [104]. Complications of the interlaminar approach are infectious complications, e.g., epidural abscesses, osteomyelitis/discitis and meningitis, and epidural hematomas [105].

As our systematic review showed, the caudal pathway was used the least often, but still in more than one fourth of the studies. Caudal epidural injections are also considered non-specific as the medication is injected very low at the level of the sacrum. Usually a larger amount of injectate is used. Caudal injections allow for multiple areas to be reached with advantageous avoidance of multiple injections. Limitations of this access route include extra-epidural needle placement, preferential flow of the contrast agent towards a non-desired direction, difficulty entering the epidural space, potential risk of dural puncture and epidural hematoma or spinal cord injury [75, 84]. Another limitation of this access route is that the injectate may not always gets as high as desired to reach pathology. This limitation was however not specifically mentioned in the included studies. It would also imply that authors mix contrast with their final injectate to detect how high the injectate passes from a caudal injection. Limitations to all three access routes include radiation exposure infection, (epidural) abscesses, meningitis, osteomyelitis, discitis, adverse or toxic effects of steroids, bleeding, as well as paraplegia, headache and pain [70, 99, 106, 107]. Overall, our findings are in agreement with a previous study, where a questionnaire was sent to 185 centers in the U.S. to record the most commonly used procedural practice [108]. This U.S.-based survey included almost all technical aspects of the procedure itself

Table 2 Arguments for and against the transforaminal (TF), interlaminar (IL), and caudal (C) injection pathway (*n* = number of studies reporting pros or cons)

Arguments	Transforaminal		Interlaminar		Caudal	
	Pros	Cons	Pros	Cons	Pros	Cons
Needle placement	Drugs at higher concentrations at the site of pathology in the anterior epidural space (<i>n</i> = 12), fewer misplacements (<i>n</i> = 1)	Difficult in case of foraminal stenosis (<i>n</i> = 2)	Correct placement in >90 % (<i>n</i> = 3), loss of resistance technique correct in 70–87 % (<i>n</i> = 3)	Correct placement in only 60–75 % (<i>n</i> = 3)	Correct placement with fluoroscopic guidance in 98 % (<i>n</i> = 1)	Incorrect placement in 14–44 % of patients (<i>n</i> = 5); intravenous leakage of steroids in up to 40 % of patients (<i>n</i> = 1)
Concentration of drugs at site of lesion	Lower dose of drugs needed (<i>n</i> = 27), less steroid side effects (<i>n</i> = 2)	Spread of the drug over a wide area, not directly at a single affected nerve route (<i>n</i> = 1)	Epidural injected drug flows freely (<i>n</i> = 1)	Medication might not reach target due to scarring, stenosis (<i>n</i> = 1)	Push injection and better diffusion of steroids in the area affected (<i>n</i> = 1),	
Complexity of procedure	Higher complexity is justified but fluoroscopic guidance reduces risk for complications (<i>n</i> = 3)	Higher complexity (<i>n</i> = 11); increased radiation exposure (<i>n</i> = 2)	Less than TF (<i>n</i> = 6)	Higher than C (<i>n</i> = 5)	Complexity of procedures: C < IL < TF (<i>n</i> = 5)	
Costs	Lower than surgery (<i>n</i> = 1)	Higher than IL or C (<i>n</i> = 2)	Lower than TF (<i>n</i> = 1)	Higher than C (<i>n</i> = 1)	Low (<i>n</i> = 1)	
Complication	Minimal adverse reactions (<i>n</i> = 3); rate 5–10 % (<i>n</i> = 2); Steroid side effects in 10 % (<i>n</i> = 1), Fluoroscopy reduces risk for intravascular injection (<i>n</i> = 2) and puncture of dura (<i>n</i> = 1); risk for dura-puncture: C < TF < IL (<i>n</i> = 2)	Potentially severe spinal cord trauma (<i>n</i> = 6); increased risk for intravascular injection, spinal cord trauma at level S1 in 11.2 % (<i>n</i> = 1); Post-puncture headache more frequent (<i>n</i> = 2),	Rate lower than TF (<i>n</i> = 5), post-puncture headache fewer than TF (<i>n</i> = 2), puncture of dura rare (<i>n</i> = 1), post puncture headache rare (<i>n</i> = 1)	Infections and epidural hematomas with severe spinal cord compression and paraplegia	Low complication rate (<i>n</i> = 6)	Minor complications vasovagal reaction 2.5 %, pain exacerbation 3.5 %, facial flush 2.5 % (<i>n</i> = 1); intravenous needle placement 14 % (<i>n</i> = 1)
Special Indication	For neural foraminal stenosis (<i>n</i> = 1); for localized nerve root compression (<i>n</i> = 1)		Axial pain (<i>n</i> = 1), upper lumbar central canal stenosis (<i>n</i> = 1)	May not be appropriate for unilateral pain (<i>n</i> = 1)	Multilevel or single central canal stenosis (<i>n</i> = 2)	

as well as medication used, but found no clear-cut consensus as to the ideal method to perform epidural injections.

Unfortunately, the U.S.-based survey did not provide a detailed evaluation of the three different access routes. Consequently, our study evaluated the level of injection in relation to the pathology and found that the injection was performed at the level of the lesion in most studies. This was true for both interlaminar and transforaminal injections. An exception was the caudal approach. All such studies use the same technique and the injection is inherently performed caudal to the lesion. To our knowledge, no other study has systematically evaluated the level of injection in detail.

An assessment of the choice of access route revealed a change in preferences over time. In the past, the caudal approach was the most frequently chosen injection route whereas the transforaminal route is the most prevalent today.

Our study has limitations. First, all literature search strategies include the inherent risk of failing to detect relevant articles. However, a structured search was performed by a professional librarian and several online libraries were included for maximum coverage of the literature. A total of more than 1,200 articles were identified and analyzed. Second, only articles in English or German were included. This represented a possible selection bias because relevant articles written in other languages (e.g., French, Spanish, Japanese, etc.) were absent. However, this is a minor issue as the bulk of medical literature is written in (or translated into) English. Third, sub-analyses of outcome or efficacy of the different access routes was not performed due to the paucity of such information in the literature. Fourth, information on who performed the procedures was not available in most studies. Thus, differences between practitioners (e.g., radiologists, anesthesiologists, physiatrists and pain management specialists) could not be evaluated. Last, there are more interesting questions regarding spinal injections which were, however, beyond the scope of this work; e.g., about criteria of success, causes of failure, complications dependent to the pathological state, or about the precise indications and efficiency according to the clinical syndrome. Unfortunately, our feeling is that evidence in literature seems to be very weak regarding those questions.

In conclusion, the most commonly used access routes for epidural drug injection are the interlaminar and transforaminal pathways at the level of the pathology. Transforaminal routes are being performed with increasing frequency in recent years.

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